My name is Jane Teta. I am a Principal Scientist with Exponent, a consulting firm based in Menlo Park, CA. I have worked for many years with the American Chemistry Council both in my capacity as Director of Epidemiology for Union Carbide Corporation and in my present position as a consultant in epidemiology and risk assessment. I have numerous publications related to ethylene oxide (EO) and risk assessment, including the cohort mortality study of Union Carbide (UCC) EO workers. I am co-author of two prior EO risk assessments based on the NIOSH original mortality cohort study and the UCC study. One of my more recent publications addresses the potential biases associated with using background leukemia incidence rates in conjunction with estimates of relative risk from a cohort mortality study to calculate lifetime excess risk, as was done in this cancer risk assessment with respect to all lymphohematopoietic cancers. In the past I have served as a consultant to EPA's Scientific Advisory Board, particularly in the areas of risk assessment and early life exposures. While I have contributed substantially to ACC's comments, the opinions I offer today are my own, based on my experience and personal research.

For many years I have been a strong proponent for a greater role of epidemiology data in regulatory risk assessment and congratulate the Agency for recognizing the value of human data for all aspects of risk assessment, including dose-response assessment. I also agree with EPA that the NIOSH study is well done and includes an exposure assessment that makes this study suitable for dose-response assessment.

I do have serious concerns, however, about how the Agency interprets the large body of epidemiology studies and the methodology employed for risk estimation. It is my recommendation that the SAB Panel carefully consider in their deliberations the following methodological errors and overly conservative policy decisions that have resulted in a unit risk factor that is unreasonable and contrary to the scientific evidence related to EO's potency.

1. **The limited epidemiologic evidence of carcinogenicity is not strong for the following reasons:**
    a. There are 12 unique EO worker cohorts that include 33,000 study subjects, several with very long follow up, yet there is no notable statistically significant increases in any subset of lymphohematopoietic (LH) cancers or LH cancers overall.
    b. The increase in lymphoid tumors and LH cancers from the NIOSH mortality study is seen only in males in the internal exposure-response analyses but not in the large number of exposed females, who had a gradient of exposures.
    c. The small excesses from the individual studies are not statisticially significant, and the summary Standardized Mortality Ratios (SMRs) from all studies combined closely approximate 100.
    d. The studies lack consistency with respect to type of LH cancers.

2. **The Agency's dose-response assessment is based upon odds ratios (ORs) in the Steenland et al. publications not on the readily available underlying NIOSH data on individual study subjects.** The linear regression on summary ORs in which the highest dose group is excluded is an invalid method for estimating dose-response, as can be verified, if one were to use the data on individuals from the NIOSH mortality database. Furthermore, dropping the highest dose group is inappropriate; it eliminates 30% of the cases, and leads to an overprediction of risk.

3. **Using LH cancers as a response, which includes numerous distinct diseases - the leukemias, non-Hodgkin's lymphoma, Hodgkin's lymphoma and multiple myeloma - sacrifices validity for sample size.** Using the underlying data to which I have access, it can be shown that leukemia and multiple myeloma have an inverse relationship with exposure in this updated NIOSH mortality database.

4. **It is has been shown in a recent publication I coauthored that using incidence background rates with relative risk estimates from a mortality study to calculate excess lifetime risk relies on an untested assumption and can lead to substantial bias.**

5. **The default potency adjustments for early life exposures are not scientifically justified based on what is known about age-related differences in response to exposure to alkylating agents, endogenous production of EO and detoxification of EO.**

6. **The proposed unit risk factor is totally inconsistent with the NIOSH mortality study upon which it is based.** It would predict close to 200 LH cancer deaths in the NIOSH cohort in which there were 37 observed. It even exceeds the upper bound of the observed of 51.

Thank you for the opportunity to offer these comments. I would be pleased to share these comments in writing to the SAB prior to the January meeting.